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TITLE: EARLY DETECTION OF BREAST CANCER ON MAMMOGRAMS USING: PERCEPTUAL FEEDBACK, COMPUTER PROCESSED IMAGES AND ULTRASOUND

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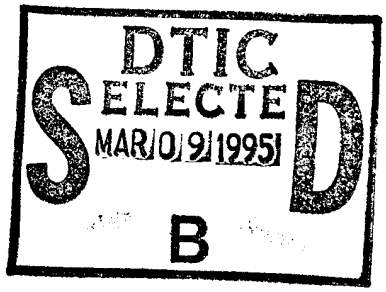

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13. ABSTRACT *(Maximum 200 words)* Three approaches are being explored for improving the detection of small tumors in the breast: (1) Perceptual feedback to decrease errors in missing tumors that are actually visible on the initial screening mammograms. The observers head-eye-position is recorded while viewing mammograms and the gaze where the eye-position dwell time is concentrated, will be feedback to the observer. The reduction in the number of incorrect decisions with bio-feedback is being studied. (2) Computer processing of screening mammograms is being developed. Computer-aided-detection of clusters of microcalcifications and the relationship between breast carcinoma and the parenchymal pattern associated with the nodular and homogeneous tissues on the mammogram are being studied. The mammogram is finely digitized (42m) with 16-bit depth. This wide dynamic range may facilitate identification of microcalcifications in high and low optical density regions of the mammogram. (3) Ultrasound echoscanning mammography is under development. Wavefront distortion of acoustic waves in breast tissue presently limits the resolution of ultrasound mammography. Existing compensation algorithms correct for the phase distortion of the receiving waveform, however from our studies of *in-vivo* ultrasound breast data amplitude distortion of the wavefront is a more serious limitation. New algorithms are being developed to correct for these amplitude distortions in ultrasound mammography.

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Peter Slack 1/30/95

PI - Signature Date

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Early Detection of Breast Cancer on Mammograms Using: Perceptual Feedback, Computer Processed Images and Ultrasound
Peter Bloch, Ph.D., Principal Investigator

ANNUAL REPORT

Early Detection of Breast Cancer on Mammograms Perceptual Feedback,Computer Processed Images and Ultrasound

Grant # DAMD 17-93-J-3014

Principal Investigator: Peter Bloch, Ph.D.

Early detection of breast cancer results in significantly higher success rates in the treatment of the disease. For example, lumpectomy and definitive radiation therapy of breast lesions, <1 cm in diameter, results in a 10 year disease free survival greater than 95 percent. The goal of this project is to improve the detection of small non-palpable lesions when the treatment is most likely to be successful. Three methods for improvement in the detection of small lesions are being explored in this study. These include:

Project 1A: Perceptual Feedback as an Aid to the Early Detection of Cancer on Mammograms,
Project 1B: Digital Image Processing of Mammograms, and
Project 1C: High Resolution Ultrasound Mammography.

In summary the major accomplishments during the year include:

- An extensive database of high and low resolution digitized clinical mammograms was established that consists of 87 mammographic examination each involving two films; a cranial-caudal and a oblique view. The clinical database has pathology confirmed abnormal lesions (34 microcalcifications, 28 masses) and 24 normals. This extensive database is required to test the efficacy of improving detection of lesions on mammograms both by perceptual feedback (project 1A) and computer image processing and feature extraction (project 1B).
- Hardware and software has been developed for the computer display of high resolution digitized mammograms
- Hardware and software has been developed for recording of eye-position of observers while reading mammograms
- Contrast resolution in breast ultrasound imaging has been shown to be significantly restored using a phase deabberration algorithm (project 1C).
- Deaberration of wavefront distortion due to refraction of ultrasound energy in breast tissue has been identified as a major source of image artifacts. Algorithms for the removal of the refracted energy in these images are being explored.

The progress during the year on these projects are presented in this annual report.

Grant # DAMD17-93-J-3014

Project 1A: Perceptual Feedback as an Aid to the Early Detection of Cancer on Mammograms.

Project Director Harold L. Kundel, M.D.

INTRODUCTION: RESEARCH OBJECTIVES

The true sensitivity of screening mammography is unknown but is estimated to be between 85% and 90% (Bird et al. 1992). This means that competent readers miss 10% to 15% of tumors that are actually visible on the mammograms. Bird et al. (1992) estimated that about half of the missed tumors were "misinterpreted", that is, a suspicious region on the mammogram was reported as negative for cancer and half were "overlooked", that is, nothing suspicious was reported. Kundel, Nodine and Carmody (1978) have found that radiologists actually give a prolonged look to most tumors that are not reported. Eye-position recording during search can be used to identify regions in the image that received prolonged attention and are reported as normal. The reader can then be shown these regions and asked to re-evaluate the decision about the image. The use of this perceptual feedback has been shown to improve the detection of lung tumors (Kundel et al.,1989,1990). We plan to apply the perceptual feedback method to reading mammograms and test it in a case controlled study.

The following research objectives have been defined.

Aim 1. Develop a computer display for mammograms that matches the grayscale properties of the display to the contrast discrimination function of the observer's eye and that displays multiple images for within breast and between breast comparison.

Aim 2. Interface a head-eye-position recording system to the display.

Aim 3. Develop and digitize a set of mammograms with barely visible visual cues for tumor.

Aim 4. In a case-control study, compare detection performance with and without eye-position feedback.

PROGRESS REPORT:

Aim 1. Mammogram Display

The mammography display station has been implemented using a SUN SPARC 10 platform, Dome video controller boards and Tektronix monitors. The original 1800 x 2200 x 8 matrix displays were not able to properly interface to the Sun platform at the time, so the display matrix of the monitors was altered to 2048 x 2048 x 8. The monitors have been analyzed using a UGG ES2110 Telemicroscope Photometer to ensure that the manufacturer's stated performance specifications and our mammography display requirements have been met. A major advantage afforded by these monitors is the high number of displayed pixels and horizontal and vertical scanning spot uniformity, providing high resolution imagery to the edges of the active display areas. This was considered a necessity due to the nature and size of the targets (microcalcifications) that may be present in breast tissue. The monitors have been extensively tested for intensity uniformity, geometric distortions, intensity output characteristics, and for MTF characteristics over the center and corners of the display areas. Both monitors met or exceeded our requirements for mammography display.

The modification of the aspect ratio of the active display areas from 4x5 to 1x1 (square) has prompted us to modify the display strategy. The icon views (see figure 1) were removed from the display area. Reference to other related studies or cases will be done, when necessary, through a reference table that is visible on demand.

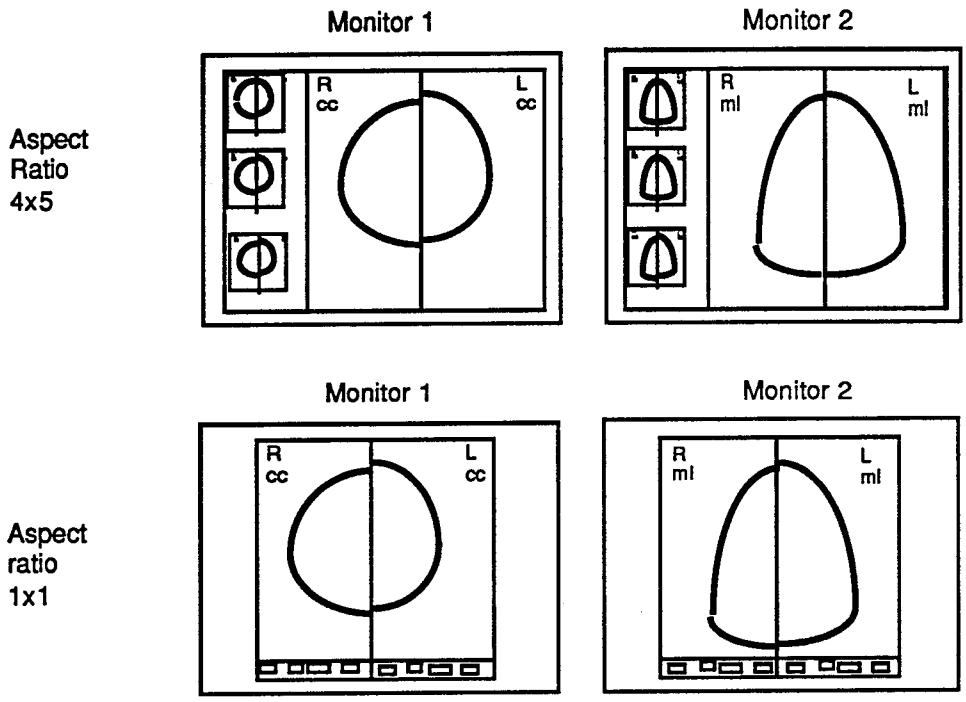

figure 1.

Initially, mammograms will be viewed by a set of observers who will have various display options available to them. We hope to ascertain from the initial data those display parameters that observers prefer. Displayed images can be manipulated by the user in various ways. The images can be viewed in reduced size, scale size, and zoomed. The reduced size is sometimes necessary to fit an entire breast image into the designated window, especially for the larger breast images. The zoom option is useful to examine the finer detail of a selected region, and can be useful in examining microcalcifications. All zoom-in operations are limited by the available pixels in the digital image. No pixel replicating is permitted. Also, the intensity characteristics of the display can be modified by adjusting the intensity window width and window center. These options are considered to be part of the minimal configuration that an observer will require while viewing digital mammograms. Additional user selectable display operators may be added to facilitate diagnosis at a future date. This will depend upon comments from observers in the initial part of the study. Viewing parameters derived from the protocol stated above will direct the software development and viewing parameters used during the eye position recording sessions to follow.

Aim 2. Eye-position Recording During Search

The eye and head position monitor obtained from the Applied Science Laboratories (ASL) has been tested and calibrated. A segment of a room dedicated to eye position data collection has been configured specifically for mammogram reading. Observer preferences such as ambient lighting, monitor placement, optimal observer-monitor viewing distance, and the user interface have been determined and tested.

Accuracy measurements have been made and have been found to be satisfactory when an observer is viewing a single display monitor. Modifications to the hardware configuration of the headband mounted magnetic and optical sensors have been necessary to obtain the required accuracy when two display monitors are used. These modifications were minor and were performed with the help and cooperation of the manufacturer of the eye position recording equipment (ASL). Figure 2 graphically depicts the typical errors associated with observer eye position data. The ellipses represent the 95% confidence interval of the eye position for a series of trials in which observers viewed 9 dots on the high resolution display.

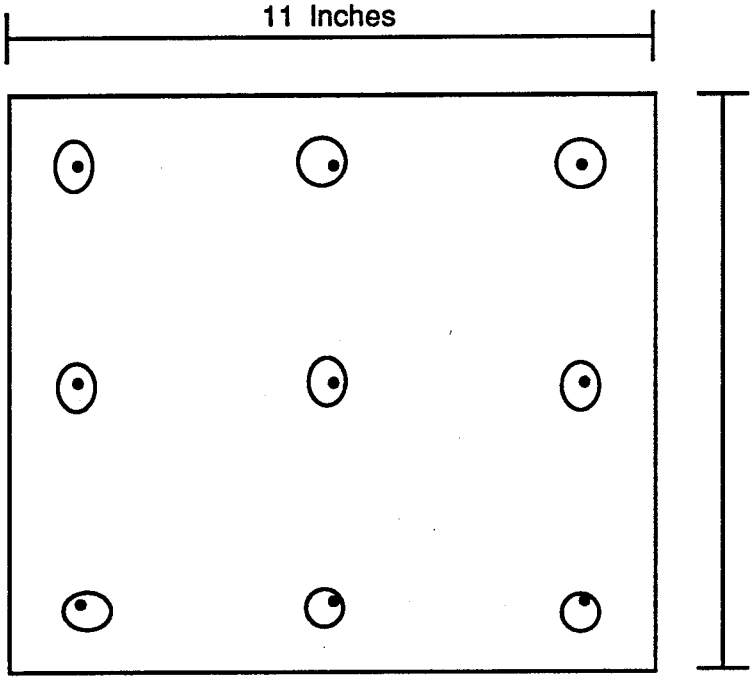

figure 2

Aim 3. Identifying Difficult Mammograms

Dr. Orel has assembled a set of 87 mammograms consisting of 34 cases with validated calcifications, 28 cases with validated masses without microcalcifications and 25 case matched, control images. The matching of controls is by age, sex, and major incidental image features. The validity of the normal images was determined by stability of the image findings for at least two years prior to the test mammogram. The images have been digitized using the DBA digitizer and the Lumisys digitizer and stored in the image archive (see the report of project 1.B for details about the digitizers). The images are being read by three experienced mammographers on film, and on the display station using images

digitized by each of the digitizers. The readers responses are being recorded using the following format which is consistent with the receiver operating characteristic (ROC) analysis.

Reading Format: You will receive a questionnaire for recording your responses. We are most interested in masses and microcalcifications and your reading for each case must use the following format.

Case XX

Calcification is	Calcification is	A mass is	The mass is
1 definitely present	1 definitely malig	1 definitely present	1 definitely malig
2 probably present	2 probably malig	2 probably present	2 probably malig
3 possibly present	3 possibly malig	3 possibly present	3 possibly malig
4 probably absent	4 probably benign	4 probably absent	4 probably benign
5 definitely absent	5 definitely benign	5 definitely absent	5 definitely benign

Location UO UI LO LI Location UO UI LO LI

Other findings

You must indicate if calcification or a mass is present or absent **for every case.** If you score a 1,2 or 3 for calcification or mass, you must indicate whether you think that it is benign or malignant. Your rating should express your confidence in your diagnostic opinion. *Please try to use the full scale for your responses.*

This study is currently in progress and when completed each case will have 9 readings (3 readers x 3 modes). A subset of these cases will be selected for the work in Aim 4.

PLANS FOR THE NEXT GRANT YEAR.

Aim 4. In a case-control study, compare detection performance with and without eye-position feedback.

Two groups of radiologists (3 experts and 3 non-experts) will view the mammograms while eye position is recorded. For each case they will report if the image is normal or if it contains the features of cancer. They will be asked to give their confidence in that decision (high, medium, low). If the image is thought to contain cancer features, they will mark the location using track ball controlled cursor. Immediately after making the decision they will be shown the image again and asked to revise their decision, if necessary. Half of the time, the second look will contain perceptual feedback, that is, it will highlight areas that received prolonged visual attention. Half of the time there will be no feedback - just a second look. After six weeks has elapsed, the test set will be shown again with the feedback and no feedback situation reversed. The diagnostic accuracy with and without feedback will be compared using the jackknife method of ROC analysis (Dorfman et al. 1992).

PUBLICATIONS AND ABSTRACTS

Kundel HL, Nodine CF, Orel SG, Barudin JL, Toto L. Computer assisted visual search in mammography. Radiology 1994;193(P):475.

REFERENCES

Bird RE, Wallace TW, Yankaskas BC. Analysis of cancers missed at screening mammography. Radiology 1992;184:613-617.

Dorfman DD, Berbaum KS, Metz CE. Receiver operating characteristic rating analysis: Generalization to the population of readers and patients with the jackknife method. Invest Radiol 1992;27:723-731.

Kundel HL, Nodine CF, Carmody DP. Visual scanning, pattern recognition, and decision making in pulmonary nodule detection. Invest Radiol 1978; 13:175-181.

Kundel HL, Nodine CF, Krupinski EA. Searching for lung nodules : Visual dwell indicates locations of false positive and false negative decisions. Invest Radiol 1989;24:472-478.

Kundel HL, Nodine CF, Krupinski EA. Computer-displayed eye position as a visual aid to pulmonary nodule interpretation. Invest Radiol 1990;25:890-896.

Metz CE. ROC methodology in radiologic imaging. Invest Radiol 1986; 21:720-723.

Project 1B: Digital Imaging Processing of Mammography Films.
Project Director: Peter Bloch,Ph.D

Research Objectives

Early detection results in significantly higher success rates in the treatment of breast neoplasms (Tabar et al.,1992). Currently mammography examinations are the only proven diagnostic procedure for detecting early breast cancer in asymptomatic women (Moskowitz,1984,Kopans,1984 and Feig,1988). The goals of this research project are to improve the detectability of breast lesions using; (1) computer assisted identification of clusters of microcalcifications on mammograms and (2) computer identification of stromal or parenchymal patterns on mammograms that are associated with breast lesions.

Clusters of microcalcification on mammograms is a radiographic feature often identified in early stage breast cancer (Sickles,1986). Approximately 30-50% of the breast carcinomas are detected by microcalcification on mammograms and 60-80% of biopsied confirmed breast carcinomas show microcalcification on histopathology samples. Thus reliable identification of small clusters microcalcification is a major importance in screening women for early stage disease.

Recent studies from the University of Chicago report 85 percent true microcalcification identification on mammograms using computer-aided detection of microcalcification (Wu et al.,1992,Nishikawa et al.,1993,and Ema et al.,1993). The mammograms used in the Univ. of Chicago studies were digitized at 100-175 microns with 10 bits of dynamic range. In an attempt to improve on the computer-aided detection of microcalcification we have tried to preserve the spatial resolution and latitude existing in the acquired screen-film combination by digitizing the mammograms at 42 microns with 16 bit of dynamic range.

Progress during the year:

The major accomplishments during the past year has been in creating the tools for clinical application of high resolution digital mammography. Software and hardware tools for archival and retrieval of large data files i.e. 50 megabytes in size are now available for routine use. The software for rapid display of digitized mammographic images with user selected contrast and magnification has been developed using the Interactive Data Language, IDL, package which is readily transportable to different computer platforms.

A database of clinical mammograms was established. Dr. Susan Orel, a mammographer, identified 87 clinical mammograms; twenty-five normals, thirty-four with histopathology confirmed microcalcifications and twenty-eight with solid tissue masses. Each mammogram was scanned twice with two different microdensitometers: (1) Lumisys-100 microdensitometer, using a100 micron pixel size and 12 bit dynamic range and, (2) a DBA microdensitometer with a 42 micron pixel size and 16 bit gray-scale. The digitized images were stored for archival on an optical disk. The size of the database of digitized mammography images is approximately 6 gigabytes.

The performance characteristics of each microdensitometer are summarized below:

(A) LUMISYS-100 MICRODENSITOMETER

The microdensitometer employs a 2 mW helium-neon laser beam. Precision mirrors mounted on a precision galvanometer movement is used to sweep a 100 micron light spot across the image plane. The light transmitted through the film is detected with a photomultiplier tube, the signal from which is logarithmically amplified and digitized. Linear regression analysis of the microdensitometer output with optical density is shown in fig. 1. The maximum signal intensity occurs at approximately 2.5 OD, corresponding to a useful dynamic range of 11 bits. However the noise evaluated from the analysis of the relative standard deviation in the output from a region of interest, ROI, of 10,000 pixels increases from approximately 0.3% at 2 OD to 0.9 % at 2.5 OD which further reduces the useful dynamic range of the scanner.

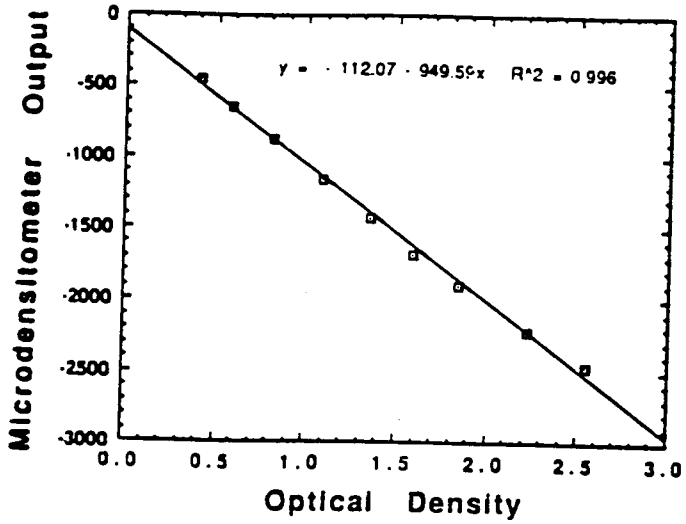

Fig.1: Lumisys Microdensitometer output with Optical Density

The modulation transfer function,MTF,for the microdensitometer was determined by taking the Fourier transform of a line spread function derived from the gradient of a measured edge spread function. The edges of square cut-outs in opaque films, 4 OD, were scanned to measure the edge spread function. The edge spread function was found to be nearly the same for all the edges of the square cutouts. The calculated MTF is shown in fig.2. The highest spatial frequency is the Nyquist cutoff frequency,5 cycles/mm, associated with the 100 micron pixel size.

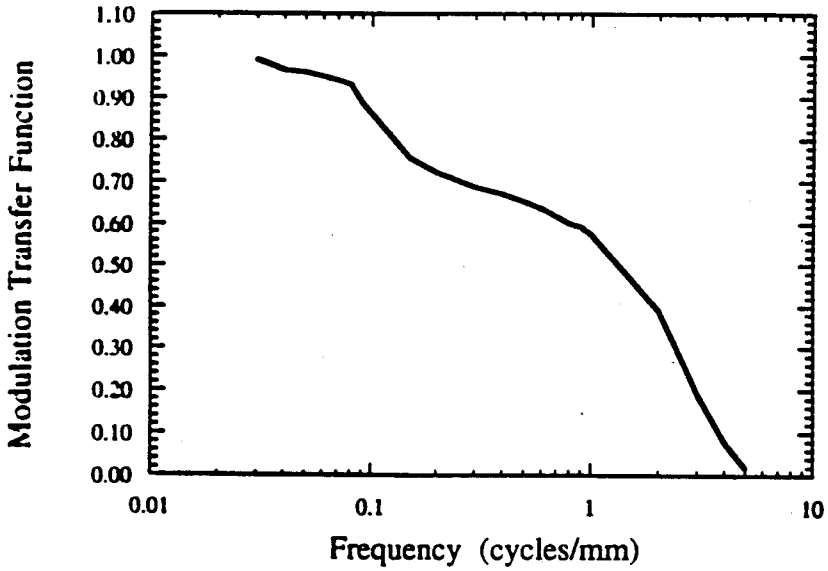

Fig. 2 Modulation Transfer Function for Lumisys Microdensitometer

(B) DBA MICRODENSITOMETER

The DBA microdensitometer scans the image plane with a 42 micron wide line light source obtained from a temperature controlled masked straight fluorescent tube. The light is detected with a 6048 linear array CCD. An image is digitized by moving the film across the line source. Digitizing a 10x12 inch mammogram requires approximately 22 seconds.

The output of the densitometer is exponential in the optical density range of 0- 4 OD (fig. 3). Routine clinical mammograms contain regions of high density thus the wide range of digitization is important for preserved all the information on the original image.

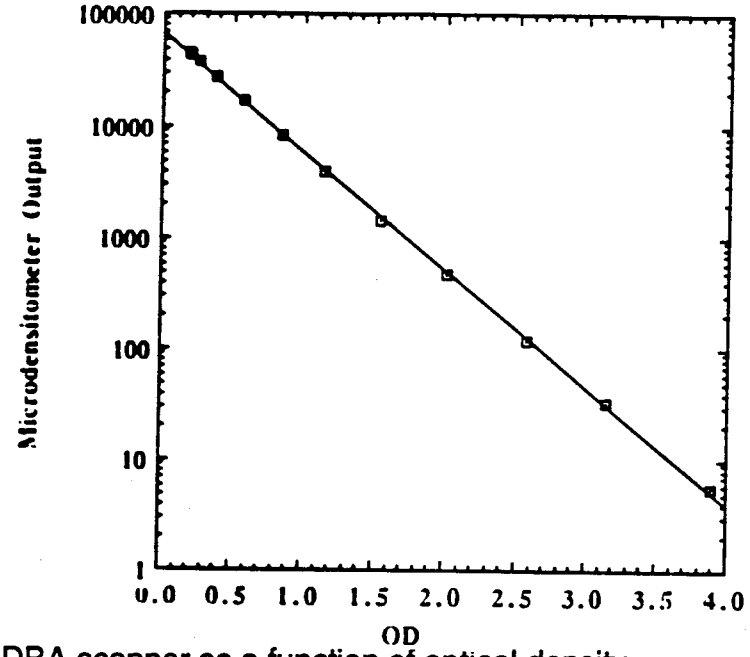

Fig. 3 Output of DBA scanner as a function of optical density

The MTF for the densitometer were derived from the measured edge profile along a single 42 micron wide scan line. The measured edge was found to depend on the edge of the square cutout scanned. Fig. 4 shows that in the direction of the light source the edge is blurred, and sharp in the direction that the film is being scanned. The light in the direction of the line source is scattered, producing glare,whereas in the direction that the film moves the registration of the light source and detectors eliminates the effects of glare.

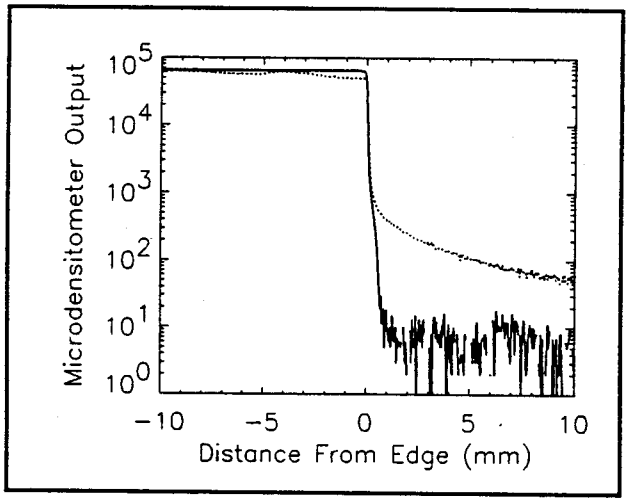

Fig. 4. Edge measured with the DBA microdensitometer. Scanned in the direction of the line light source,(solid line),and perpendicular to the light source (dotted line).

The edge spread function, ESF, (the measured output as a function of distance from the edge normalized to the maximum output) in the direction of the line light source was found to be nearly independent of irradiated area, over the range studied 1-25 cm^2. This area was defined by cutouts in opaque films. In addition, placing neutral density filters between,0.25-0.98 OD, over the square opening did not significantly alter the measured ESF.

The MTF derived for edge spread functions are shown in fig. 5. The high frequency cutoff is at the Nyquist frequency 11.9 cycles/mm corresponding to the pixel size of 42 microns. The MTF at lower frequencies is significantly reduced In the direction of the line source. Thus the degradation in image quality associated with the presence of glare is predominately in the low frequency components. This would suggest that the effects of glare on the image can be significantly reduced by filtering the low frequency components measured in the direction of the light source.

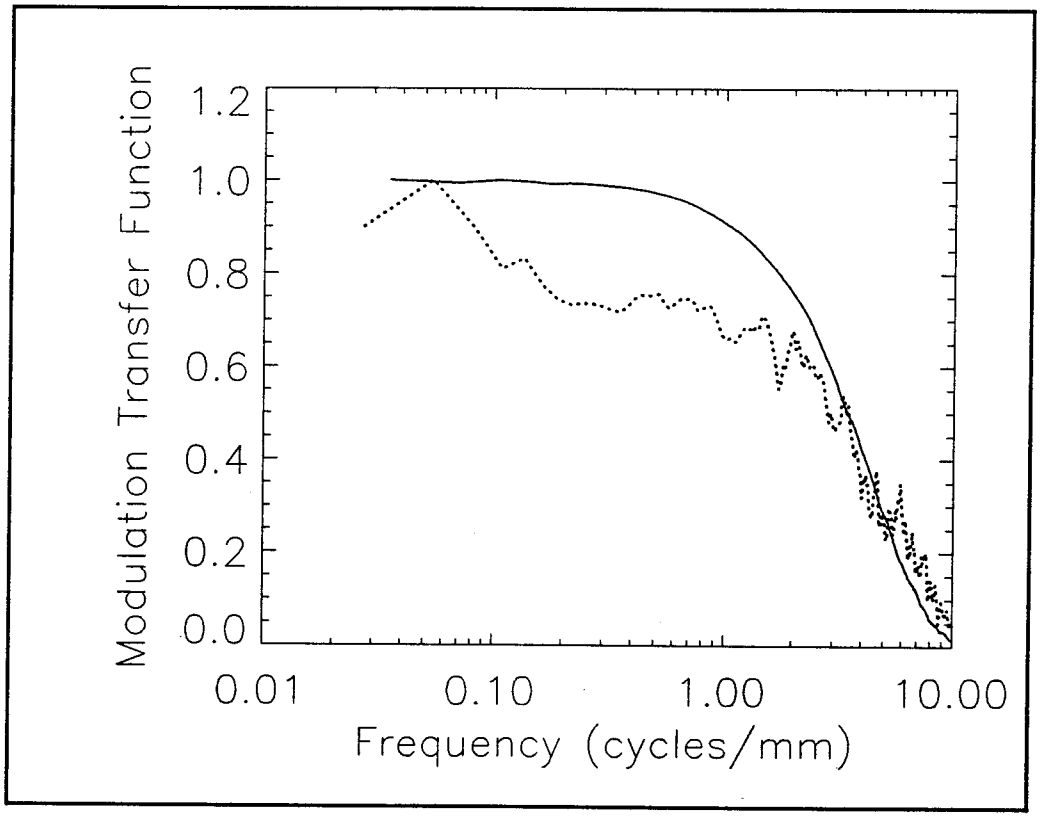

Fig. 5: MTF for the DBA microdensitometer. Scanned in the direction perpendicular to the line light source,(solid line),and in the direction of the light source (dotted line).

Figure 5 also indicates that the measured noise in the direction of the line source is much greater than the noise measured in the direction perpendicular to the light source. This noise could arise from fluctuations in the; (1) light intensity along the light source, (2) cross talk between elements in the large linear CCD detector array, and (3) analog to digital conversion.

Figure 6 shows the relative noise power spectra measured in three regions: (1) within the square cutout region containing no film, (solid line), (2) in an opaque area lateral to the square cutout in the direction of the line source, (dashed line), and (3) in an opaque area perpendicular to the direction of the line source, (dotted line). In region 2, the noise is associated with glare, which decreases with increasing spatial frequency. In region 3, the noise is a low level white noise. In region 1, superimposed on the noise due to glare is shot noise associated with the linear array CCD detector.

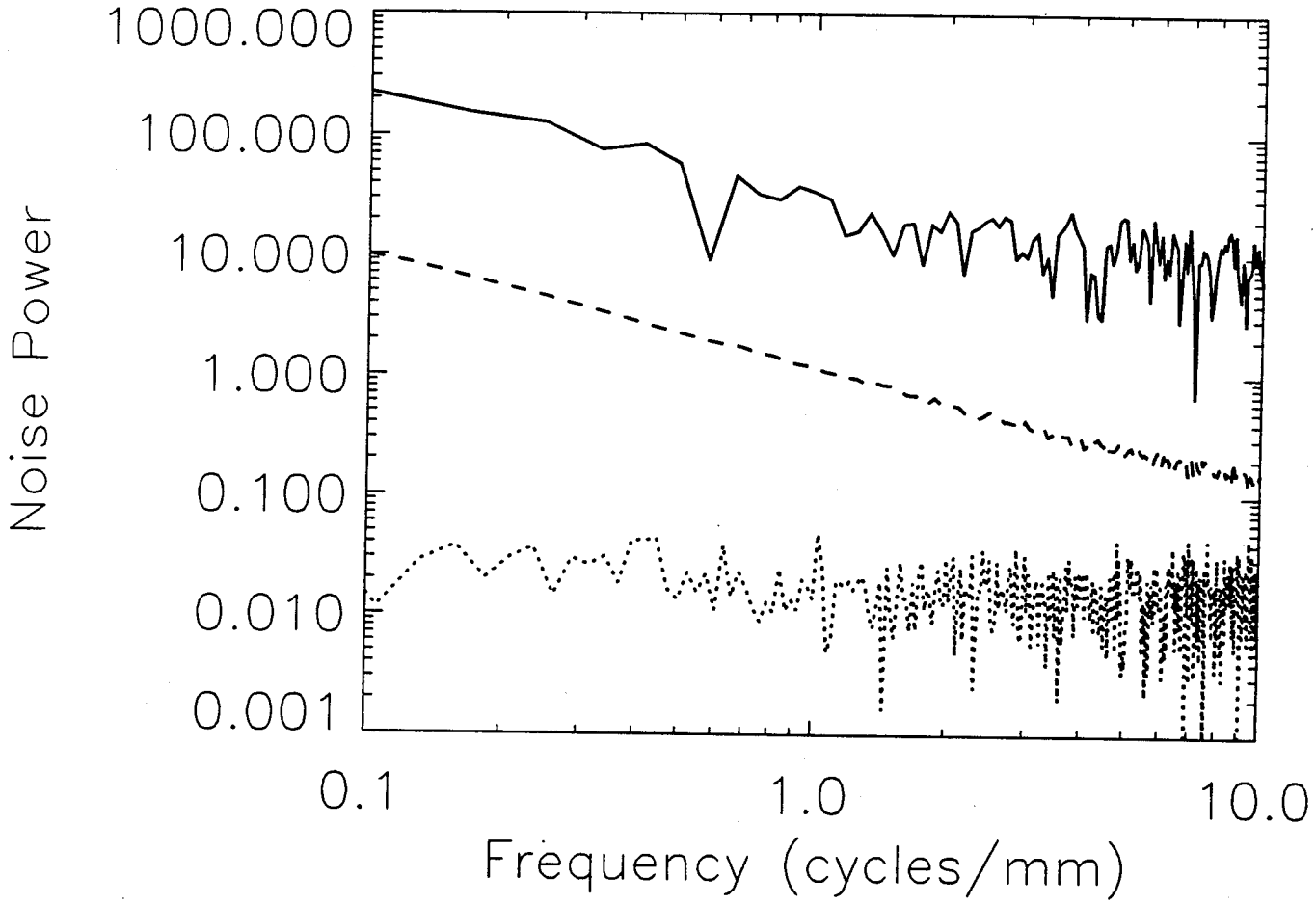

Fig. 6 Relative noise power for the DBA scanner. Solid line, region of high light signal, and opaque regions; (dashed line), lateral to the square cutout in the film in the direction of the light source, and (dotted line) perpendicular to the direction of the linear light source.

The implication of noise on visual perception of microcalcification and masses on digitized images is not clear at this time. However, the directional dependence of the noise may have some implications in computer aided detection,CAD,of clusters of microcalcification. The shot noise associated with the signal intensity may have implication in CAD of microcalcification in regions of dense breast tissues.

CONCLUSION

A comparison of the two MTF's in figures 2 and 5 for the Lumisys and DBA scanners respectively demonstrates the improvement in the physical performance of the higher resolution scanner. In project 1B the effects of preserving the spatial details in the digitized image on radiologist performance in identifying clustered microcalcifications and masses on mammograms is being investigated.

Algorithms for computer aided detection of clusters of microcalicifications, including; local thresholding methods,(Chan et al., 1988),neural networks,(Wu et.al,1992),and fractal analysis,(Lefebvre et al.,1992) will be evaluated using the digitized mammography database obtained with the high and low resolution scanners.

REFERENCES:

Chan,H.P.,Doi,K.,Galhotra,C.,Vyborny,C.J.,MacMahon,H. and Jokich,P.M. (1987) "Image feature analysis and computer aided diagnosis in digital radiography. 1. Automated detection of microcalcifications in mammography",Medical Physics,**14**, 538-548

Ema,T.,Doi,K.,Nishikawa,R.M. et al., (1993) "Computer-aided diagnosis of clustered microcalcification in digital mammograms: Reduction in false-positive findings using edge-gradient analysis" (1993) Radiology Supp. **189**,186

Feig,S.A.,(1988) "Decreased breast cancer mortality through mammographic screening: Results of clinical, trails," Radiology,**167**,659-665

Kopans,D.B., (1984) "Early breast cancer detection using techniques other than mammography," Am. J. Roentgenol. **143**,465-468

Lefebvre,F.,Benali,H., and Kahn,E. (1992) "Fractal analysis of clustered microcalcifications in digital mammograms" Acta. Stereol. **11**, 611-6616

Moskowitz,M. (1984), "Mammography to screen asymptomatic women for breast cancer," Am. J. Roentgenol. **143**,457-459

Sickles,E.A.,(1986) "Mammographic features onf 300 consecutive nonpalpable cancers" Am. J. Roentgenol.**146**,661-663

Tabar,L.,Fagerburg,G.,Duffy,S.W.,Day,N.E.,Gad,A. and Grontoft,O. (1992) Update of the Swedish two-country program of mammographic screening for breast cancer, Radiol. Clin. N.America, **30**,187-210

Wu,Y.,Doi,K.,Giger,L., and Nishikawa,M.,(1992),"Computerized detection of clustered microcalcifications in digital mammograms: Applications of artificial neural networks," Medical Physics,**19**,555-560.

Project 1C: Research in High Resolution Ultrasound Mammography

Co-Investigator: Bernard Steinberg,Ph.D

INTRODUCTION

The objective of the ultrasound echoscanning mammography research is detection and classification of breast lesions the order of 2 mm in size and differentiation of such small tumors from cysts. The primary obstacle is poor image quality (artifacts, false targets) caused by distortion to the wavefront when the tranducer is made large enough (5-10 cm) to achieve the desired lateral resolution (0.2 mm) and sidelobe level ($\sim$ -60 dB) at chest wall. In a prior experimental study we obtained a massive database on wavefront distortion of acoustic waves as they passed through *in vivo* breast. Analysis of those data was the first essential task under this program and it was completed last year. Refs. [1-2] are the remaining publications from that work.

That study was followed by acquisition and analysis of 2-D data. Testing of various data-adaptive signal processing methods to counter wavefront distortion was also accomplished and the limitations determined [3-4]. New algorithmic development is underway to counter what we believe to be the primary obstacle [4]. Theory and modeling of 2-D scattering has been undertaken as a parallel effort to the experimental work [5-6].

Continuing is the study of practical high resolution arrays of large size [7]. Under development is sensitive experimental facilities designed to measure the effectiveness of the deaberration procedure as well as to test the sidelobe properties of designs of the large arrays required for ultrahigh resolution [8-10].

SUMMARY OF TASKS

1. **Evaluation of existing wavefront distortion compensation algorithms.** A large number of algorithms have been published by our laboratory and others. All or nearly all can be shown to be phase correction algorithms, that is, they compensate for the distortion to the phase of the received waveform but not the amplitude or modulus. We had earlier evaluated phase aberration correction on 1-D *in vivo* data obtained from mammography patients at HUP. The results were helpful but inadequate; these algorithms, which all operate upon the transverse spatial correlation function of the distorted wavefront, reconstruct a main beam reasonably well, but do not result in the low sidelobes required for successful differentiation of tumors from cysts. Thus, this genre of algorithms, which is the largest class of existing algorithms, are inadequate.

This year we worked with 2-D, wideband *in vitro* data and remeasured the utility of these algorithms. See next section for results.

2. **Acquisition of 2-D data.** Wavefront distortion sources disperse energy volumerically and not only in the plane of the transducer. Our earlier HUP 1-D data analysis showed that the algorithms required would necessarily be 2-D algorithms. To insure that our earlier conclusions drawn from the 1-D data were sound, it was necessary to acquire 2-D wavefront data. It is also necessary to have such data to test the algorithms that will develop from the data analyses. For this reason we developed a collaboration with Professor Robert Waag at the University of Rochester who was set up to make 2-D wavefront measurements of acoustic waves passing through *in vitro* breast specimens. We took 2-D large-aperture transmission data, developed analytical computer tools, and analyzed the data this past year.

The basic 2-D measurement system is as follows. Briefly, wideband 3.7 MHz ultrasonic waves radiated from a hemispherical transmitter and the wavefronts after propagating through breast specimens were measured by a large 1-D, horizontal receiving aperture. The array was translated in the elevation dimension to form a large 2-D aperture (96mm by 46mm). The element spacing was 0.7 mm in the array dimension and 1.4 mm in elevation. Breast samples with various thickness were placed between the source and the receiving aperture.

From these 2-D data we obtained various image displays, including isometric, maximum projection, contour mapping and 1-D slices and projections. From these we could isolate and measure incoherent scattering (caused by density variations in tissue) and coherent interference (caused by refraction from dense bodies). We found

i. The images artifacts (false targets) are 10-20 dB weaker than the target.

ii. The scatter spectrum is generally 20-30 dB weaker than the target.

iii. The angular scattering spectrum and the images artifacts that result from coherent interference occupy about the same space in the image, a few degrees around the target image.

iv. Phase deaberration algorithms reduce the energy in the scatter spectrum by 15-20 dB.

v. The same algorithms do not reduce the false targets.

vi. However, phase deaberration algorithms fold the eliminated scattered energy into the target image, thereby building it up and increasing the contrast between target and false target. The experimental improvement in the ratio is 7 dB.

3. **Development of stronger method of deaberration.** Phase deaberration appears adequate for scattering but not for refraction. Refraction causes multiple arrivals at the receiving array, each of which gets imaged as a target. We now believe that we must develop and apply a three step procedure:

i. Phase deaberrate to materially reduce the scattered energy. Use existing algorithms.

ii. Identify the false targets.

iii. Eliminate them by some form of interference cancellation.

For i, the existing algorithms (time delay (TD) compensation, TD plus backpropagation, time reversal mirror, spatial correlation, etc.) appear adequate. We are now working on ii and iii. For ii, we have found that when the target and its cluster of false targets are viewed ultrasonically from slightly different positions the target tends to retain its shape and location while the false targets do not; both their shapes and locations change. We have developed a spatial diversity procedure which appears to distinguish between real and false targets. We break the received data set into four parts, each from a different quadrant of the array. By comparing the four images the distinction is usually clear. We plan to try to develop automatic methods to identify the true targets. One procedure to be tested is multiplication of the four images. Only the geometrically stable image (the real target) should survive.

For iii, we are adapting the body of techniques called coherent interference cancellation developed for radar and communications in the presence of jammimg. We have tried one experiment on aperture data (measurements directly from the array) and one in the image domain. The first is called adaptive nulling, in which nulls are created in the radiation pattern in the directions of the false targets. The second cancels beams of false target energy using *a prori* knowledge of the diffraction pattern of the transducer array. Both very crude experiments give rise to optimism, showing about 7 dB improvement. This will be actively pursued in the remaining year.

4. **2-D transducer array analysis.** The 2-D deaberration problem demands large, 2-D transducer arrays (up to 10 cm), highly thinned (or sparse) for practicality and cost control. We have continued our study and analysis of such arrays this year and are developing procedures for what we call the square-root-of-N array, where N is the number of elements and receiver channels required by conventional design. For a 10-cm array operating at 7.5 MHz, N is of the order of 10^6, which is much too large both technologically and economically. A square-root-of-N array would require about 1000 elements and channels, which industry could manage. Results to date favor the highly thinned, periodic deterministic array over the equally highly thinned random array. The ideas on this subject were presented in a conference paper earlier this month [7].

5. **Experimental facility.** Development of a 3-D synthetic aperture water tank experimental facility is continuing. It will serve two functions: Precision measurement of radiation patterns of large (up to 10 cm), 2-D, highly thinned transducer arrays; and echo tests of deaberration

algorithms on phantoms. The 3-D precision micropositioner was received in November 1994 and is being assembled. The computer control software for the system and the data acquisition software are completed and have been installed. System testing should be completed in the Spring.

REFERENCES

[1] Q. Zhu and B. D. Steinberg, "Wavefront Amplitude Distribution of the Female Breast," J. Acoust. Soc. Am. 96, 1-9 (1994).
[2] Zhu, Q., Steinberg, B. D. and Arenson, R., "Correlation Distance Measurement of the Female Breast, " Accepted for publication by JASA subject to revision (1993). Resubmitted 1994.
[3] Q. Zhu and B. D. Steinberg, "Modeling, Measurement and Correction of Wavefront Distortion Produced By Breast Specimens," Proc. IEEE Int'l Symp. Ultrason. Ferroelec. Freq. Cont., Cannes, Nov. 1994.
[4] Q. Zhu and B.D. Steinberg, "First Experiments of Coherent Cancellation of Refractive Artifacts," AIUM Convention Proceedings (March 1995).
[5] B.D.Steinberg, "Scattering from a Multiple Random Phase Screen Model of an Random Inhomogeneous Medium," to be submitted to JASA.
[6] B.D.Steinberg, "Contrast and Resolution as affected by Scattering in Inhomogeneous Tissue," AIUM (American Institute of Ultrasound in Medicine) 39th Annual Convention, San Francisco, CA, 26-29 March 1995.
[7] Jodi Schwartz and B.D.Steinberg, "The characteristics of interference patterns produced by widely spaced, ultrawideband arrays," URSI/IEEE Ant. Prop. annual meeting, Boulder CO, Jan.1995.
[8] Q. Zhu, "Design Specifications of Radiation Pattern Measurement System," VFRC PR#63, 106-113, June 1994.
[9] H. Chen, "Micropositioning System for the Purpose of Radiation Pattern Measurement," VFRC PR#63, 114-119, June 1994.
[10] W. Tang, "Development of Digitizing System in Ultrasound Project," VFRC PR#63, 120-126, June 1994.